Ninety-fourth Advisory Committee on Animal Feedingstuffs meeting
30th October 2024 – Online meeting

ACAF	FSA
Nick Jonsson (Chair)	Nathan Allen
Martin Briggs	Sarah Bannell
Emily Burton	Edward Fuller
Katrina Campbell	Rebecca Greenaway
Hannah Kane	Beth Hall
Susan MacDonald	Natasha Hawkins
Chris McAlinden	Lindsay Holden
Donald Morrison	Emily Hudson
Derek Renshaw	Michelle Hutchinson
Mike Salter	David Kovacic
Adam Smith	Kaila Lee
Christel Wake	Francisco Matilla
Helen Warren	Barry Maycock
Nick Wheelhouse	James Metcalfe
	Lucy Smythe
	Johann Trotter
	Alba Ureña Rusillo

1. Apologies

Matthew Fisher sent his apologies.

2. Welcome

The Chair welcomed members of the Committee, Secretariat and observers from the Devolved Administrations.

3. Risk Assessment update

The Regulated Products Team Leader Francisco Matilla-Garcia provided an update, highlighting the number of upcoming publications and when they will be published. The first internal assessment performed by the Secretariat will be brought to the December ACAF meeting for members to review and provide feedback. Members were also informed that future drafts brought to the Committee will be formatted according to the templates used for publishing.

4. Policy update

Animal Feed Policy Advisor, Beth Hall, provided an update for policy, updating the Committee on the number of applications received since the last meeting, of which there have been seven. The Committee were informed that the validation of applications has been handed over from Policy to the Regulated Products Service Delivery (RSPD) team. A presentation was then given detailing the complete Regulated Products cycle to provide a recap for members and to provide more information relating to the post-risk assessment phase.

5. Minutes from 93rd Meeting

The Committee reviewed the minutes from the 93rd ACAF meeting and provided feedback to be reviewed by the Secretariat.

6. Dossier for assessment: RP1649 Patent Blue V

No conflicts of interest were declared for this item.

An applicant was evaluated for Patent Blue V. The additive falls under the category "sensory additive", functional group "colourants, substances that add or restore colour in feedingstuffs". The applicant requests an authorisation for use in all non-food producing species.

The ACAF reviewed the data provided for identity and characterisation, noting that the additive presented in the dossier did not have the same specifications as the original authorisation, **the applicant would be asked to provide further data to demonstrate that the additive is the same as described in the original authorisation, in the absence of this data the applicant would be asked to provide a complete dossier for assessment**. Members reviewed the data provided for particle size distribution and the justification for not providing data on dusting potential, noting that the data on particle size distribution was not suitable for assessment and concluding that data on dusting potential was required for assessment. **The applicant would be asked to provide data on particle size distribution and dusting potential for each form of the additive, ensuring suitable methods are followed.** The Committee reviewed the applicant's justification for omitting impurity studies from the dossier, concluding that these studies are a requirement under Regulation 429/2008 and would be required to allow a comprehensive assessment of the additive. **The applicant would be asked to provide impurities data for the additive in each of its forms.**

The Committee noted that the applicant did not provide an updated manufacturing process for the additive, despite the changes in the specifications of the additive. **The applicant would be asked to provide detail of the changes made to the additive since the original authorisation.** The flow chart for the process was not in sufficient detail for assessment and did not contain detail of the critical control points for the process. **The applicant would be asked to provide an updated flow chart for the manufacturing process including the critical control points.** Members noted that quality assurance documentation had not been provided for the manufacturing process, **the applicant would be asked to provide quality**

assurance documentation for the manufacturing process, demonstrating that the additive is produced according to feed hygiene regulations. The physico-chemical properties of the additive were assessed by Members, who noted that the stability trials performed were unsuitable for assessment owing to poor reporting and unclear presentation of results. **The applicant would be asked to provide updated data to demonstrate the stability of the additive**. Methods of analysis had not been included for assessment; **the applicant would be asked to provide the methods of analysis to allow a comprehensive assessment of the additive.**

As the additive described in the dossier does not have the same specifications as the additive currently authorised. The Committee could not conclude on possible genotoxicity as full reports of relevant studies had not been provided. **The applicant would be asked to provide studies concerning either the additive described in the application or the currently authorised additive to demonstrate safety for the target species and the consumer.** No studies were provided for safety for the user/worker, owing to the absence of data the Committee concluded that the additive should be considered a respiratory and skin sensitiser and an eye and skin irritant.

7. Dossier for assessment: RP1888 Lactiferm (*Enterococcus faecium* NCIMB 11181)

Martin Briggs declared an indirect conflict of interest and remained in the meeting for this item.

An application was evaluated for Lactiferm® (*Enterococcus faecium* NCIMB 11181). The applicant requests a new authorisation of the additive for use in all growing poultry, and ornamental birds. The additive falls under the category “zootechnical additives” and functional group “gut flora stabiliser”. The Committee reviewed this dossier and carried out an assessment on the efficacy section.

The Committee assessed the six studies provided in this application, commenting that they were well conducted with comprehensive reports. However, members noted that the demonstration of reduced feed intake while maintaining performance was inconsistent among studies, with only a couple demonstrating efficacy. It was also noted that all the trials were for broilers that had been fed mash only diets which is not typical for UK broiler production. However, as it was specified that the additive is not intended to be used in pelleted diets, members accepted the studies performed on mash. The applicant had referred to spraying the additive on pelleted feed and this would typically be an aqueous solution, but the only aqueous solution stability testing done was in drinking water and only for 48 hours, whereas sprayed feed should typically be stored for months. Members stated that three out of the six trials show a positive effect for efficacy, however, the remaining three studies showed little potential for efficacy.

It was concluded that not enough evidence for efficacy has been provided in chickens for fattening to be able to extrapolate to all growing poultry and ornamental birds. **The applicant would be asked if they wish to provide additional efficacy data that would support this application. If additional data are not currently available, the Committee will be unable to conclude on the efficacy of the additive. The applicant would also be reminded that there is also the option of withdrawing the application at this stage.**

8. Dossier for assessment: RP2074 FUMzyme (Fumonisin esterase)

Adam Smith declared a direct conflict of interest and left the meeting for this item.

The FUMzyme® additive is a product consisting of fumonisin esterase. The additive is categorised as a technological feed additive in the functional group: substances for reduction of the contamination of feed by mycotoxins: substances that can suppress or reduce the absorption, promote the excretion of mycotoxins, or modify their mode of action. The enzyme is produced by a genetically modified (GM) yeast strain, *Komagatealla phaffii* DSM 33835.

Identity and characterisation of the additive was assessed by the Committee. The Committee identified that the batch information was acceptable however **the applicant would be asked to provide clarity regarding the testing for yeasts and moulds.** Members noted that the strain was acceptably characterised using whole genome sequencing. The members wanted to ensure no AMR genes of concern were found in the additive so the whole genome sequencing and associated information would be reviewed offline.

The Committee noted there appeared to be missing information in the HACCP plan for sections contained in the manufacturing process. Members noted they would also like to see evidence of accreditation of the in-house laboratories or method validation. **The applicant would be asked to provide a full HACCP plan and confirm the accreditation of the quality assurance laboratories.** Members noted that the data submitted by the applicant appeared to demonstrate stability however further information around humidity is required. In addition, members would like to understand what containers the product would be sold in. **The applicant would be asked to provide humidity information for the stability data along with clarification on what containers the product would be marketed in. The applicant would also be asked to provide an example label of the additive.** It was unclear what product was used to test particle size, therefore **the applicant would be asked to confirm the product for which particle size was measured.**

Members discussed the importance of demonstrating that the metabolites and/ or degradation products of fumonisin were less toxic than fumonisin itself. **The applicant would be asked to perform a literature search to determine the potential toxicity of the metabolites and degradation products.** Members stated that testing the undiluted fermentation product for safety was sufficient and given the results of the safety testing, maximum intake levels are not required. Members queried the use of a positive control in the bacterial reverse mutation assay which was not recommended in the guidance. **The applicant would be asked to clarify why this specific positive control was used.** Members could not conclude on eye irritancy using the test provided. No studies for skin sensitisation were provided, therefore the additive should be considered a potential skin sensitiser. The additive is also an enzyme product, therefore should be regarded as a potential respiratory sensitiser. Members confirmed that this additive would be classed as non-irritant to the skin. **The applicant would be asked to confirm proposals for personal protective equipment and update the MSDS accordingly.**

The Committee could not conclude on efficacy highlighting some concerns around the dairy cattle and fish studies. Members also discussed the efficacy in relation to need. **The applicant would be asked to explain the homogeneity of the additive in feed and information on how the additive is added to pelleted feed. The applicant would also be asked to provide further information on the quality assurance systems of the efficacy trials.**

Addendum notes:
Members reviewed the molecular characterisation information provided offline and concluded that the AMR genes of concern in the GM vectors were shown to be removed. There was sufficient evidence to show that the production strain was not present in the final product.

9. Response to RFI: RP1055/RP1582 Huvezym neXo

Adam Smith declared an indirect conflict of interest and remained in the meeting for this item.

Members were satisfied with the testing provided for *Bacillus cereus*, as well as the HACCP plan and certification certificates. The applicant provided further clarity on their use of 40% overage to cover any loss following the addition of granulation agents and during granulation itself. Members accepted that the overage covers any loss in enzyme activity during storage, ensuring that a batch will have an enzyme activity of not less than the values declared on the label if used at expiry of the shelf-life. The Committee were satisfied that homogeneity had been demonstrated following a recalculation of the co-efficient of variation across each of the whole of the batches sampled. The applicant accepted the Committee's conclusion on pelleting stability up to 85°C for 20-25 seconds and provided an updated label to include this.

The Committee discussed the applicant's request to extrapolate tolerance from laying hens to breeder poultry, highlighting that according to EFSA guidance this extrapolation is not possible without an additional study in breeding hens considering only performance endpoints. **The applicant would be asked to further justify their stance that the additive is safe for use in all poultry, such as using available non-clinical data to identify safe levels in feed.** Members had previously noted that some details were missing from the tolerance study for sows and minor pig species. The applicant has now provided the methods for weighing and backfat analysis, as well as information on the frequency distribution of return to oestrus intervals. The applicant was also asked to provide analysis on the dosing solutions used in the 90-day sub-chronic toxicity study. In their response it was stated that the dosing solution was prepared weekly and stored at 2 – 8°C. The Committee noted that analysis of dosing preparations is required to confirm concentrations and stability under the conditions of storage. Members concluded that the study does not need to be repeated, however **the applicant is asked to provide evidence to demonstrate the stability of the dosing solution at 2 – 8°C.**

Members discussed the justification provided by the applicant regarding the lack of a positive control for clastogens without metabolic activation in the *in vitro* mammalian cell micronucleus test. The positive controls provided do not address the requirement

in the guidelines that “positive controls for both clastogenicity and aneugenicity should be used in metabolically competent cells that do not require S9”. **The applicant is asked to provide further justification for the absence of a positive control.** Skin irritation studies were provided for the solid and liquid forms of the additive and the Committee concluded that neither are irritant to skin. However, as the additive is an enzyme product, it is considered to have the potential to cause sensitisation by exposure to skin or by inhalation.

A replacement efficacy study for weaned and suckling piglets was provided by the applicant for which the Committee concluded that efficacy was convincing. The Committee are now therefore able to conclude that the additive is efficacious in weaned and suckling piglets. Further clarification was provided for one of the trials for chickens for fattening, allowing members to conclude positively on efficacy for chickens for fattening. The Committee had also asked for clarification regarding calcium levels in the feed in one of the trials for laying hens, but were able to conclude positively as there were three acceptable trials demonstrating efficacy. After seeking more information on the sow trials, the Committee concluded that the additive is efficacious in sows. Although the Committee was of the view that the individual sow should not (strictly speaking) be considered the experimental unit in this study, it was agreed that the applicant had achieved the closest possible design that could be achieved in a commercial setting for this class of animals, given regulations about individual stallings of sows in the EU.

10. Response to RFI: RP1070/RP1072 Avatec

No conflicts of interest were declared for this item.

The ACAF reviewed the study provided to demonstrate genetic stability, concluding that the data adequately demonstrated the production strain’s stability. Members reviewed the updated flow chart provided for assessment, concluding that the detail provided was adequate for assessment. The applicant had clarified the parameters of the pelleting stability trials, and the Committee concluded that no further information would be required from the applicant at this stage.

11. Response to RFI: RP1512/RP1696 *Bacillus velezensis* ATCC PTA-6737 (PB6)

Emily Burton declared a direct conflict of interest and left the meeting for this item and the following item.

An RFI referring to two applications containing the same additive (*Bacillus velezensis* ATCC PTA-6737) was sent to the applicant as there were conflicting statements in the identity sections. The applicant provided clarification regarding the presence of AMR genes, as well as the absence of plasmids. The Committee were satisfied with the applicant’s response and had no further queries.

12. Response to RFI: RP1696 *Bacillus velezensis* ATCC PTA-6737 (PB6)

As in the previous item, Emily Burton has a direct conflict of interest and therefore remained out of the meeting.

Members were satisfied with the updated label including a statement on the compatibility of the additive with halofuginone, as well as the exposure time used during pelleting. The Committee concluded that changes in inclusion rates of the ingredients used for the growth media constitutes a change in the manufacturing process and this results in an increase in the minimum concentration of the active agent in the additive. Members agreed with EFSA that these are minor changes in the manufacturing process and do not raise any safety concerns.

The applicant has provided a HACCP for the manufacturing plant Geneferm; however, the **applicant would be asked to provide assurance certification for Geneferm.** The Committee noted that some of the MSDS provided do not match the ingredient list provided in the applicant's previous ACAF RFI response. **The applicant would be asked to clarify the discrepancies between the ingredient list and the MSDS provided.**

The applicant was asked to provide a rationale as to why the additive has been classed as a respiratory irritant. They confirmed that the additive is a respiratory irritant, however the applicant also mentioned that the additive should be considered a respiratory sensitiser due to its proteinaceous nature. **The applicant would be asked to provide a rationale for the additive being classed as a respiratory irritant, not a sensitiser.** The Committee were satisfied with the studies provided relating to skin and eye irritation and concluded that the additive is non-irritant to the eyes and skin.

The Committee discussed the efficacy reports provided, concluding that the **applicant would be asked again to provide the original report from the research provider, with appropriate redaction if required.**

13. Draft safety assessments: RP1070/RP1072, RP1154, RP1243, RP1258, RP1298, RP1317, RP1341, RP1366, RP1400 and RP1421

Members were presented with draft Committee's Advice documents for applications RP1070/RP1071/RP1072, RP1243, RP1258, RP1317, RP1366, RP1393 and RP1400.

The Committee was also presented with the final drafts of the Committee's Advice document for applications RP1154, RP1298 and RP1341. The Committee provided feedback on final corrections and approved the opinions to be finalised and sent to Risk Managers.

14. Updated EFSA guidance

Members reviewed the updated EFSA guidance and provided feedback on whether these documents are adequate to inform assessment of GB applications.

15. Any other business

An update on upcoming applications was provided.

Next ACAF meeting: 18th December on Microsoft Teams.